REMARKS

I. Preliminary remarks

Applicants acknowledge with thanks the withdrawal of various rejections and objections from the previous action. Applicants traverse the new non-statutory, obviousness-type double patenting rejection and new rejections under §112, second paragraph, and request reconsideration.

Although a previous objection to the title was overcome by amendment, Applicants have amended the title herein again, to make the title more consistent with the current claim set and arguments presented herein.

Some of the claims have been amended to insert or amend clauses as suggested by the Examiner in the Office action, as explained below in greater detail. (See, e.g., amendments to claims 46, 62, 67, 81-82, 89-92, and 94.)

Claim 68 has been rewritten in independent form, introducing the limitations of its parent claim, because it recites a different category of inhibitor molecule than the molecules recited in the parent claim.

Claim 77 has been rewritten in independent form, incorporating the limitations of the claim from which it previously depended.

Claims 87-88 have been amended to replace the word "patient" with "mammalian organism that is a human" because the parent claims use the phrase "mammalian organism" and not for reasons related to patentability.

Claims 97-98 have been amended so that they do not depend from canceled claims.

Applicants have added claims 99-112 by this amendment, but these are not new to this application. Rather, claims 99-112 are largely identical to previously presented claims that were canceled *solely* to expedite allowance of other claims, in response to Office actions in which other claims had been indicated as allowable. The Examiner has now rejected the allowed claims, rendering moot the Applicants reasons for the previous claim cancellations. Therefore, Applicants have reintroduced the canceled claims for reconsideration by the Examiner or eventual reconsideration by the Board of Appeals. (The

Applicants have tried to incorporate the Examiner's suggestions for other claims into these new claims also.) The relationship between the new claims and previously canceled claims is set forth in the following chart:

New claim	Previously presented claim
99	50
100	51
101	52
102	53
103	61
104	62
105	63
106	64
107	54, 56
108	55
109	57
110	58
111	59
112	60

Applicants also have added new claims 113-126 in this amendment.

New claim 113 is an independent claim with a concise preamble and two steps: a screening step and an administering step. (Claims 67, 68, and 89-92 have similar structure.) The Markush group of inhibitors recited in claim 113 is the same group recited in numerous other claims. (Compare, e.g., claims 67, 81, and 85.) Claim 113 finds support throughout the specification, including at paragraphs [0047], [0050], [0052], [0057-0060] of the published application (US 2004/0208879).

New claim 114 has an administering step that specifies administering the same Markush group of inhibitors, and further specifies a monitoring step. The monitoring steps in claims 114, 115, and 117 find support throughout the specification, including at paragraph [0051] and [0058-0060] of the published application.

New dependent claims 116, 118, and 121 specify a screening step or an identifying step that finds support throughout the specification, including at paragraphs [0038], [0058-0060] of the published application.

Support for human or humanized antibody, as recited in claims 120 and 123, is found, e.g., at paragraph [0047] of the published application.

Claims 119, 122, and 124-126 specify limitations that are already recited in other claims.

None of the amendments introduces new matter.

II. The rejections under 35 U.S.C. 112, second paragraph, should be withdrawn.

At page 3 of the action the Office alleged that claims 46, 48, 62-64, 67-70, 72-75, and 77-98 were indefinite. Applicants respectfully traverse.

A. The acronyms in the claims do not render the claims indefinite.

The Office rejected claims 46, 69, 74, and 79, alleging that the use of acronyms without first defining what they represent in the independent claims is indefinite. (Action at p. 3.) Applicants traverse this rejection.

"Office policy is not to employ *per se* rules to make technical rejections. ... The test for definiteness under 35 U.S.C. 112, second paragraph, is whether 'those skilled in the art would understand what is claimed when the claim is read in light of the specification.'[*Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986)." See MPEP §2173.02. The rejection here appears to be based on an inappropriate *per se* rule relating to acronyms. Applicants note that chemical formulae are routinely presented in claims using letters such as C, H, N, and O to represent various elements, without spelling out the words that these letters represent. These are examples of abbreviations, acronyms, or symbols that are not indefinite.

Turning to the specifics of this rejection, the acronyms used in the rejected claims are "PAL-E" and "VEGFR-1" and VEGFR-2." Even without resort to the specification, there is context provided by the Markush group language used to introduce these terms: "a blood vascular endothelial marker antigen." (See, e.g., Jalkanen declaration at paragraph 2.3.) A scientist in the field of the invention at the time of filing would have been familiar with the proteins expressed on blood vascular endothelial cells to which these acronyms refer, and would not have needed the acronyms spelled out in order to give meaning to the claims. (See, e.g., Jalkanen declaration at paragraphs 2.4 to 2.10.) Thus, the claims (even standing alone) are not indefinite.

Moreover, definiteness need not be judged in a vacuum but in the context of the specification, and the specification provides additional context for the acronyms. For example, with respect to VEGFR-1 and -2, the specification uses additional names by which these receptors are known. ("VEGFR-1/Flt1 (fms-like tyrosine kinase-1) and VEGFR-2/Kdr/Flk-1 (kinase insert domain containing receptor/fetal liver kinase-1)." See paragraph [0012] of the published application, US 2004/0208879.) With respect to all three proteins, publications that would have been known to people in the field are cited in the specification to further identify the proteins. (See, e.g., published application at paragraphs [0015], [0024], and [0240].) In fact, the scientific community commonly used the acronyms to identify those proteins. (See, e.g., Jalkanen declaration at paragraphs 2.4 and 2.9 and appendices cited therein.)

B. The rejection alleging missing steps and limitations is moot.

The Examiner alleged that claims 46, 62, 67, 72, 73, 78, 81, 82, 85-86, 89-92, and 94 were "missing steps and limitations" and therefore indefinite. The Examiner suggested additions to claims, such as "an effective amount" and "where the inhibition of Flt4 function treats breast cancer" with respect to claims 46 and 62.

Applicants traverse the rejections because the claims as written are not *indefinite*. The claims as previously presented were understandable, even if an additional clause would further improve the claims. Applicants also disagree with any characterization that steps are missing or that the changes proposed in the Office action would constitute additional steps per se. For example, the "where" clause suggested by the Examiner states that the existing steps of claims achieve a result specified in a preamble. Also, the proposed "effective amount" and the "result achieved" clauses serve similar functions for purposes of clarity, because "effective amount" refers to an amount needed to achieve an effect (a result).

Still, to expedite allowance, claims 46, 62, and 67 have been amended to add a clause as suggested by the Examiner, rendering moot the rejection.

Claims 72, 73, 78, and 85-86 already contain clauses of the type suggested by the Examiner (e.g., claim 72: "thereby inhibiting Flt4-mediated proliferation of the blood vessel endothelial cells"), so no further amendment is appropriate or necessary.

Claims 81, 82, 89-92, and 94 already contained a "thereby" clause, but the clause in these claims has been amended herein to more closely mirror the preamble of the claim, rendering moot the rejection.

For all of these reasons, the rejection alleging indefiniteness should be withdrawn.

III. The obviousness-type double patenting rejections should be withdrawn.

The Examiner has newly rejected claims 46, 48, 62-64, 67-70, 72-75, 78-81, 83-88, 90-92, and 94-96 of the application "under double patenting over claims 1, 6, 17, 32, 38, 50-52, and 53 of" U.S. Patent No. 6,824,777 (hereinafter "the '777 patent"). Applicants disagree and request reconsideration of the rejections in view of the following remarks. The arguments below are applicable to all pending claims, unless specific claims are referred to or context clearly indicates otherwise.

A. Claims 77, 93, and 97-98 were not rejected.

At page 24 of the action, the Examiner indicated that claims 77, 93, and 97-98 were "objected to because they depend on rejected claims." However, these claims were not rejected. Claim 77 has been rewritten in independent form, rendering moot the rejection. Thus, claim 77 is believed to be in condition for allowance.

The Applicants reserve the right to rewrite claims 93 and 97-98 in independent form if the rejections of their parent claims is maintained. Because claims 93 and 97-98 are multiple dependent claims, Applicants have refrained from such amendments at this time to minimize surcharges for excess independent claims. As set forth below, the rejection is improper with respect to all rejected claims, including the claims from which claims 93 and 97-98 depend.

B. Even if claims of the '777 patent claims "encompass" pending claims, the rejection is improper.

The Examiner withdrew an indication that certain claims were allowable on the basis that "the scope of" claims 46, 62-64, 67, 72, 73, 78, 81, 83-86, 90-92, and 94-96 "is encompassed by" one of claims 1, 17, 32, 38, 50-52, and 53 of the '777 patent. (See action at, e.g., p. 4.) Even if true, the "encompassed by" conclusion would not support a rejection.

The Patent Office's reviewing court has stated that a double patenting rejection cannot be justified solely on the ground that the subject matter of a claim in a second patent or application is dominated by the claims in a first patent. See *In re Kaplan,* 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986). See also MPEP §804 ("Domination and double patenting should not be confused. They are two separate issues. One patent or application 'dominates' a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection.") To provide one example, improvements are a category of patentable invention expressly authorized under 35 U.S.C. § 101 (1999), despite the fact that an improvement will often be dominated by the prior patent upon which the improvement is made. Because "encompass" represents the consistent focus (if not the entire focus) of every one of the double patenting rejections, the rejections are improper as a matter of law.

C. Double patenting must focus on the claims of the cited patent, but the Examiner has improperly relied on the patent's specification to support the current rejection.

The current double patenting rejections are based on improper criteria. The rejections make repeated reference to *embodiments in the specification* of the '777 patent that purportedly contribute to the conclusion of obviousness. The MPEP and the Patent Office's reviewing court make clear that an obviousness-type double patenting analysis is different from an obviousness analysis. Obviousness-type double patenting analysis only involves a comparison of *claims*, and not an analysis of whether embodiments in the specification of the issued patent (which in this case is identical to the specification of the pending application) would render claims obvious. See MPEP § 804, citing *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992) (When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art.)

D. Claims reciting "blood vessel (or vascular) endothelial cells" or "blood vessels" are non-obvious over the claims of the '777 patent reciting "cells" or "endothelial cells".

All of the pending claims are directed to various methods that involve administering an inhibitor of Flt4 function to a mammalian subject having blood vessels that express Flt4 or a neoplastic disorder (or other disorder) ***characterized by expression of Flt4 in the blood vasculature*** (e.g., blood vessels, blood vascular endothelial cells, etc) of the subject. Some claims of the '777 patent generically recite "cells" or "endothelial cells."[1] The recitation of a ***specific type*** of cell is non-obvious over the generic class of "cells" recited in the claims of the '777 patent. This is particularly true where, as here, it was not obvious that blood vessel endothelial cells expressed Flt4, the target of the inhibitors recited in the claims.

The conventional wisdom regarding Flt4 expression is generally reflected in the prior art of record and is summarized by Applicant's expert, Dr. Jalkanen, in paragraphs 5.2-5.9 of her declaration. Dr. Jalkanen explains that, at the time the patent application was filed, Flt4 was generally considered to be a marker for lymphatic endothelial cells in mature organisms; Flt4 expression was thought to become restricted to lymphatics during development.

1. Summary of the Office's position/rejection.

The Office's position on this distinction between blood vessel subject matter of the claims and lymphatic subject matter of the '777 patent is repeated throughout the action, and the rejection of claim 81 will be taken as representative. (Action at pp. 14-15.) The Office rejected claim 81 based on claim 50 of the '777 patent. The Office acknowledged that claim 50 "does not recite inhibiting genesis of blood [vessels] ...." Nonetheless, the Office alleged that claim 50 rendered claim 81 obvious "**because the specification teaches** that a preferred embodiment of the invention includes lymphatic or vascular endothelial cells (column 8, line 24 of US Patent 6,824,777) **encompass the limitations** of claim 94 [sic: 80] of the instant application." (Action at p. 15, emphasis added.)

[1] Claims relating to targeting of blood vascular endothelial cells that were *allowed* during prosecution of the '777 patent *were canceled prior to issuance* because such claims are directed to a distinct invention, See amendment filed on August 28, 2003 in connection with the application preceding the '777 patent (Copy attached as Exhibit F to the amendment dated February 11, 2008. See also the certificate of correction canceling claim 7 of the '777 patent.

The Office also asserted that dependent claim 84 of the application "drawn to a tumor characterized by blood vessels that express Flt4 matching the limitations of claim 52 of the '777 patent." (Office action at p. 16.) Claim 52 of the patent specifies "a cancer characterized by lymph node metastases." (See also the rejections of claims 85 and 86 at p. 17.)

2. Proper double patenting analysis.

Neither claim 50 nor any other claim of the '777 patent discloses or suggests targeting blood vessels that express Flt4 to treat cancer. See the claims of the '777 patent and the Jalkanen declaration at paragraphs 6.0 and 6.5. The generic references to Flt4 and the specific references to lymphatic expression of Flt4 would not have suggested the present methods directed toward blood vessels that express Flt4. Thus, the subject matter in claim 81 of the present application is not obvious from the claims of the '777 patent, and the rejection is improper.

3. Errors in the Office's analysis

As explained above in detail, the mere fact that a patent claim may "encompass" the subject matter of a claim in an application is not a sufficient basis for a double patenting rejection. However, that is the essence of the Office's analysis here.

Also as explained above, it is improper to rely on the specification of a patent to support a double patenting rejection. In this respect, the present rejection bears many parallels to the double patenting rejection that the Federal Circuit *reversed* in its *Kaplan* decision, cited above. The Office had issued a patent to Kaplan on a process of making chemicals in the presence of an *organic solvent*. "Among organic solvents disclosed and specifically claimed in the Kaplan patent are two known as "tetraglyme" ...and sulfolane." In fact, two of the Kaplan dependent claims individually named these specific solvents, but no claim in the Kaplan patent called for a solvent mixture. Still, the *specification* of the Kaplan patent contained "a number of examples of mixed solvents" including (in Example 45) a specific mixture of "Tetraglyme/sulfolane." The PTO had rejected claims in the pending application because they were directed to essentially the same chemical process, though they required the use of a solvent mixture of tetraglyme and sulfolan.

In reversing the double patenting rejection, the Federal Circuit held that the mere fact that the broad process claim of the Kaplan patent requiring "an organic solvent" reads on or "dominates" the narrower claim directed to basically the same process using a specific solvent mixture does not, *per se*, justify a double patenting rejection:

> To use the words of which the board seemed to be enamored, the broader claim "embraces" or "encompasses" the subject matter defined by the narrower claim. In possibly simpler terms, one patent dominates another if a claim of the first patent reads on a device built or process practiced according to the second patent disclosure. This commonplace situation is not, per se, double patenting as the board seemed to think.

By the same reasoning, *even if* claims of the '777 patent "encompass" claims of the present application, this relationship *per se* does not justify a double patenting rejection.

The PTO's double patenting rejection in *Kaplan* was not premised wholly on the issue of encompassing/dominating claims, however. The PTO also reasoned, "Example 45 of the Kaplan patent clearly shows that the term solvent, as used in Kaplan's claims is intended to embrace the mixed solvent of Example 45. ... Surely, the tetraglyme/sulfolane solvent [example in the specification] provides some of the support for the term 'organic solvent' as used in claim 4 of the Kaplan patent." The Federal Circuit squarely rejected the PTO's use of the specification to support the double patenting rejection:

> There is no way the board could have found appellants' claimed invention to be an obvious variation of what Kaplan claims except by treating the Kaplan patent disclosure as though it were prior art. This has repeatedly been held in our precedents to be impermissible. *In re Vogel; In re Aldrich; In re Boylan*, all *supra*.

Although the *Kaplan* decision is from 1986, it is unquestionably still good law, and has recently been followed by the Board when an Examiner made a similar, erroneous double patenting rejection. In *Ex parte Engel and Diseroad*, 2008 WL 4054884 (BPAI August, 2008) (copy appended hereto), the Board followed *Kaplan* and reversed an Examiner's double rejection of claims directed to crystalline forms of an organic molecule.[2]

[2] See also *Ex parte Gewehr et al.,* (BPAI September 29, 2008); and *Ex parte Hottovy et al.,* (BPAI December 29, 2008).

In its decision, the Board noted, "There is no dispute that the patented claims are generic to claim 3 of the application, and would dominate claim 3 of the application." The Examiner's rejection was based in part on this fact, and also on the fact that the subject matter claimed in the application was described in an Example in the cited patent, and could have been claimed in that patent. However, the generic salt as claimed in the prior patent did not render obvious the crystalline form claimed in the rejected application, so the Board reversed. The fact that the Examiner could find the subject matter of the application's claim within the scope of the prior patent's claim and in a working example was not dispositive, because it is not proper to use the specification in this manner as a basis for a double patenting rejection.

The rejection in the present case is based on the same type of errors that the Board made in *Kaplan* and an Examiner made in *Engel*: focusing on an alleged "domination" or "encompassing" relationship between claims; and resorting to the *specification* for a teaching that Flt4 is expressed in blood (as well as lymphatic) vessels of cancers, a teaching that is not found in the claims of the '777 patent and is not found in the prior art. Absent improper reliance on the specification, all of the claims are directed to methods involving the targeting of Flt4 in the blood vasculature that are non-obvious from the claims of the '777 patent.

With respect to claims 84, 85, and 86, it is an error of fact to equate a tumor characterized by blood vessels that express Flt4 as "matching" a cancer characterized by lymph node metastases. The blood and lymphatic systems differ, and tumor angiogenesis is a different phenomenon from metastases through the lymphatics. (See also rejection of claim 94 at p. 23, where the Office makes a similar error.)

For all of these reasons, the Office's double patenting rejection of every rejected claim was in error, and should be withdrawn.

E. Claims reciting a step comprising screening for a condition characterized by blood vessel expression of Flt4 are non-obvious over the claims of the '777 patent.

Claims 64, 67-70, 87, 89-93, 102, 106-113, 116, 118-119, and 121-126 each include a method step involving, e.g., screening for a condition characterized by blood vessel expression of Flt4. For example, claims 90-91 each have a step that reads, "screening a human subject to identify a neoplastic disorder characterized by blood vessels that comprise

endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4)." Claim 92 has a similar step. The administering step in each of these claims is performed on a subject identified according to the first step as having such a disorder.

1. Proper double patenting analysis

None of the claims of the '777 patent teach or suggest a method that involves a step of screening a human subject to identify a neoplastic disorder **characterized by blood vessels that comprise endothelial cells expressing Flt4 receptor tyrosine kinase (Flt4).** It would not have been obvious from the claims of the '777 patent to screen subjects in this manner to identify whom to treat. See Jalkanen declaration at paragraphs 8.1 to 8.4. Thus, it is improper to reject claims that contain such a step on the ground of obviousness-type double patenting.

2. Errors in the Office's analysis

a. Errors rejecting claims 90-92

The Office cited claim 17 of the '777 patent as allegedly rendering obvious claims 90-92. Claim 17 comprises a step of "screening a mammalian subject to identify a neoplastic disorder characterized by **cells** expressing Flt4 receptor tyrosine kinase (Flt4)." (Emphasis added). It would not have been obvious from a direction to screen to identify a neoplastic disorder characterized **by cells expressing Flt4** (claim 17) to perform the more specific step of screening to identify a neoplastic disorder **characterized by blood vessels that comprise endothelial cells expressing Flt4**. See, e.g., Jalkanen declaration at paragraph 8.4.

The Examiner completely ignored this difference in the screening steps between claim 17 of the '777 patent and claims 90-92 of the present application. To ignore this difference, an unobvious difference, was clear error.

b. Errors rejecting claims 64 and 67-70.

The Examiner relied on claim 34 of the '777 patent to reject claim 64 (and apparently claim 67)[3] of the present application. The screening step of claim 34 specifies

[3] The rejection of claim 67 appears to span pages 7-9, with the last two lines of the two page rejection referring to the screening step. These two lines confusingly refer to claim 64, however.

"screening a human to identify breast cancer characterized by endothelial cells expressing Flt4." This screening step differs from the more specific step in claim 64 of screening a human to identify breast cancer characterized by **blood vessel** endothelial cells expressing Flt4. Again, the Examiner completely ignored this difference in the screening steps (this time between claim 34 of the '777 patent and claim 64 of the present application). (The Examiner characterized the screening step of claims 64 and 67 as "matching" the limitations of claim 34 of the '777", Office action at pages 7 and 9.) To ignore this difference, an unobvious difference, was clear error. It would not have been obvious from the claims of the '777 patent or the prior art to screen for breast cancer characterized by blood vessel endothelial cells expressing Flt4. See Jalkanen declaration at paragraphs 8.4 and 6.2. For the same reasons, the screening step of claim 67 would not have been obvious.

c. Errors rejecting claim 87.

Claim 87 depends from claim 85 and specifies a diagnosing step that comprises identifying a patient having a tumor characterized by blood vessels that express Flt4. The Examiner alleged that claims 52 and 50 rendered claim 87 obvious on a theory of inherency:

> claim 52 of the '777 patent reciting a cancer characterized by lymph node metastases in combination with claim 50 of the '777 patent reciting a method of inhibiting genesis of lymphatic vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in lymphatic vessels inherently encompasses the limitations of claims 87 and 88 of the instant application.
>
> (Action at p. 18.)

The lymphatic system conducts interstitial fluids (lymph) through lymphatic vessels to return the lymph to the blood circulatory system. It is distinct from the system of blood vessels that transport blood throughout the body. The Examiner provided no reasoning or scientific evidence why blood vessels that express Flt4 would be an inherent characteristic of a patient having lymph node metastases. In fact, like the other rejections discussed in this section, it is not even apparent that the Examiner has acknowledged that this difference exists between claims 87 of the application and 52 of the '777 patent.

Moreover, the principle of inherency cannot be applied to claim 87 for an additional reason; the cited patent claims (50 and 52) do not specify any diagnosing step. Even apart from the clear distinction that exists between lymphatic metastases and blood vessels that express Flt4, the principle of "inherency" cannot be used to impute a method step where none is recited. The diagnosing step of claim 87 cannot be considered "inherent" in claim 50 or 52 of the '777 patent.

d. Errors rejecting claim 89.

The Office failed to articulate the reason why claim 89 was purportedly rejected for obviousness-type double patenting, so the rejection of claim 89 should be withdrawn.

3. Conclusion

For all of the foregoing reason, the rejection alleging obviousness-type double patenting was improper with respect to claims 64, 67-70, 87, and 89-93, and should not be applied against new claims 102, 106-113, 116, 118-119, and 121-126.

F. Claims reciting bispecific antibodies are non-obvious over the claims of the '777 patent reciting an anti-Flt4 antibody.

Independent claims 46, 62, 68, 72, 73, 78, 82, 86, 90, 92, 99, 104 and 107 of the present application specify an inhibitor that is "a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen." Claims 48, 63-64, 69, 74-75, 77, 79-80, 83-84, 87-88, 93, 100-101, 105-106, 108-112, 118, and 125-126 depend from these claims, and thus also are patentably distinct for the reasons outlined below.

1. Proper double patenting analysis.

The claims of the '777 patent neither disclose nor suggest a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen. Nor do the claims of the '777 patent disclose or suggest use of such a bispecific antibody as an inhibitor. See Jalkanen

declaration at paragraphs 4.2 to 4.4. Thus, the rejection of these claims is improper, and should be withdrawn.

2. Errors in the Office's analysis

Claim 46 was the first of these rejected claims, and is representative of a repeated error by the Office rejecting claims that specify bispecific antibodies. The Examiner relied on claims 1 and 5 of the '777 patent to reject claim 46 of the patent application, asserting that "claim 5 of the '777 patent recites an anti-Flt4 antibody which is defined as a bispecific antibody or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen (column 9, lines 60-67 of US Patent 6,824,777) ..." (Office action at p. 5.)

As already noted above, resort to the specification in this way is impermissible in a double patenting analysis.

Even if it were permissible to resort to the specification in this manner, the rejection is improper because the Examiner in this instance has *misread* the specification. Dr. Jalkanen explains in paragraphs 4.4 to 4.9 of her declaration that the '777 patent describes the Flt4 antibody and the bispecific antibody as different types of inhibitors. Her analysis is summarized below. The excerpt cited at column 9 of the '777 patent simply does not *define* anti-Flt4 antibody as a bispecific antibody.

A fairer interpretation of the '777 patent starts at column 8, lines 9-16, which provides a generic statement of the invention involving *inhibitor compounds*:

> The invention also is directed to a method of treating a mammalian organism suffering from a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in cells, comprising the step of administering to the mammalian organism a composition, the composition comprising a compound effective to inhibit the binding of an Flt4 ligand protein to Flt4 expressed in cells of the organism, thereby inhibiting Flt4 function.

Anti-Flt4 antibodies are discussed at lines 55-59, in the paragraph *preceding* the paragraph cited by the Examiner, as *an example of* an inhibitor compound. There is no mention in that paragraph of bispecific antibodies:

> For therapeutic methods described herein, preferred compounds include polypeptides comprising an antigen-binding fragment of an anti-Flt4 antibody, and polypeptides comprising a soluble Flt4 extracellular domain fragment. Human and humanized anti-Flt4 antibodies are highly preferred.

The paragraph cited by the Examiner explains that another class of *inhibitor compound* for practice of the invention is the bispecific antibody:

> An expected advantage of the therapeutic methods of the invention lies in the fact that Flt4 is normally not expressed at any significant level in the blood vasculature of healthy tissues. In a highly preferred embodiment, the therapeutic compound comprises a bispecific antibody, or fragment thereof, wherein the antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen.

The paragraph plainly does not define anti-Flt4 antibody at all. Rather, the paragraph specifies another ***embodiment of inhibitor compound*** for practicing the invention. The only thing established by column 9 is that an anti-Flt4 antibody and a bispecific antibody are *different embodiments* for practicing the invention. See Jalkanen declaration at paragraph 4.8.

The allegation that the '777 patent defines an anti-Flt4 antibody as a bispecific antibody is simply a misreading of the specification. Based on a proper reading of terms, claims of the present application reciting bispecific antibodies are patentably distinct from the claims of the '777 patent reciting an anti-Flt4 antibody.

The Office also asserted that "the specification of the '777 patent contemplates using the inhibitor bispecific antibody ..." (Office action at p. 9, citing column 10, lines 4-6, of the patent. See also Office action at pp. 12 and 13.)

G. A monitoring step as recited in new claims 114-115 would not have been obvious from the claims of the '777 patent.

New claims 114-115 include a step of monitoring the progression of a therapy, the monitoring including measuring the quantity or distribution of Flt4 within blood vasculature of a human subject. As discussed above in detail, the claims of the '777 patent neither disclose nor suggest doing anything with respect to blood vessels. See also Jalkanen

declaration at paragraphs 5.1 and 9.1. For these and other reasons, no double patenting rejection should be applied to claims 114-115 (or other claims that depend therefrom).

H. The preamble of claims is a limitation that distinguishes the claims from claims of the '777 patent.

The Federal Circuit's decisions make clear that a claim's preamble constitutes a limitation when the preamble is necessary to breath life and meaning into the claim. See MPEP §2111.02 ("'If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is 'necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the balance of the claim.' *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003) (In considering the effect of the preamble in a claim directed to a method of treating or preventing pernicious anemia in humans by administering a certain vitamin preparation to 'a human in need thereof,' the court held that the claims' recitation of a patient or a human 'in need' gives life and meaning to the preamble's statement of purpose.).")

The present application contains examples where this principle surely applies. For instance, claim 81 has an administering step that specifies administering "to said mammalian organism." The preamble of the claim provides antecedent basis for "said mammalian organism" and injects additional life and meaning to the claim in specifying, "A method of inhibiting genesis of blood vessels in a mammalian organism having a disease characterized by expression of Flt4 tyrosine kinase (Flt4) in blood vessels." The purpose recited in the preamble of claim 81, and the mammalian organism to be treated, would not have been obvious from any claim of the '777 patent. (See Jalkanen declaration at paragraphs 7.1.)

The Office alleged that claim 81 was obvious in view of claim 50 of the '777 patent, which is drawn to a method of inhibiting genesis of lymphatic vessels. The Office reasoned that "the specification teaches that a preferred embodiment of the invention includes lymphatic or vascular endothelial cells (column 8, line 24 of U.S. patent 6,842,777)...." (Office action at p. 15.) As explained above, it is legal error to use a mention in the specification of the presently claimed invention as grounds for concluding that a claim is

obvious. The claims in the '777 patent are directed to a distinct invention and do not suggest the invention of claim 81.

A similar analysis applies to at least claims 82, 94, and 103, for example. See Jalkanen declaration at paragraphs 7.2 and 7.3. In fact, all claims with preambles that are distinct from subject matter claimed in the '777 patent are unobvious in view of the claims of the '777 patent.

I. Conclusion

Because the claims of the pending application recite the various non-obvious elements discussed above that are not recited in the claims of the '777 patent, the claims of the present application are non-obvious over the claims of the '777 patent. Accordingly, the various double patent rejections should be withdrawn.

IV. Request for interview

To further expedite allowance, Applicants request the opportunity to schedule an in-person interview with the Office to discuss the current rejections, at a time at which the Examiner expects to reconsider the case.

V. Conclusion

In view of the above amendments and remarks, Applicants believe that the pending application is in condition for allowance.

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Respectfully submitted,

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